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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/611,652	07/07/2000	Richard J. Zeman	001290.091198	8034

1912 7590 06/18/2003

AMSTER, ROTHSTEIN & EBENSTEIN  
90 PARK AVENUE  
NEW YORK, NY 10016

EXAMINER

HUI, SAN MING R

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 06/18/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application N .

09/611,652

Applicant(s)

ZEMAN ET AL.

Examiner

San-ming Hui

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 31 March 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5, 8, 10, 21-31 and 37-46 is/are pending in the application.
- 4a) Of the above claim(s) 2, 3, 5, 8, 10, 21-31, 38, 39 and 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 4, 37, 40, 42-46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 31, 2003 has been entered.

Claims 1-5, 8, 10, 21-31, and 37-46 are pending.

The elected species is clenbuterol, as stated in response filed September 10, 2001, Paper No. 5.

Claims 2, 3, 5, 8, 10, 38, 39, and 41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species.

Claims 21-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions.

Claims 1, 4, 37, 40, 42-46 are examined to the extent they read on the elected invention and specie.

The outstanding rejections under 35 USC 102(b) is withdrawn in view of the applicant's remarks filed March 31, 2003.

The outstanding rejection under 35 USC 103 over Sayers et al. is withdrawn in view of applicant's remarks filed March 31, 2003.

***Claim Rejections - 35 USC § 102***

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 37, 40, 44-46 are rejected under 35 U.S.C. 102(a) as being anticipated by Zeman et al. (Experimental Neurology, 1999;159:267-273).

Zeman et al. teaches a method of treating spinal cord injury by employing clenbuterol to increase the locomotor functions in patients with spinal contusion injury to the T8-T11 regions (see abstract and page 269, col. 2, second paragraph). Zeman et al. also teaches the dosage of clenbuterol as 9mg/L (this is a dosage equivalent to 1mg/kg/day in human) (See the abstract).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1,4, 37, 40, and 42-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zeman et al. and Etlinger et al., references of record.

Zeman et al. teaches a method of treating spinal cord injury by employing clenbuterol to increase the locomotor functions in patients with spinal contusion injury to the T8-T11 regions (see abstract and page 269, col. 2, second paragraph). Zeman et al. also teaches the dosage of clenbuterol as 9mg/L (See the abstract).

Etlinger et al. teaches a method of treating spinal cord injury in animal employing clenbuterol in a dosage of 9mg/L, equivalent to 1mg/kg/day human dosage (See page 11 – page 14). Etlinger et al. further teaches administration of clenbuterol in a dosage of about 0.5 to 1000.0  $\mu\text{g/day/kg}$  to treat scoliosis (See page 5, line 27; page 9, line 18-19; also page 11, example 1). Etlinger et al. also teaches the spinal cord injury is at the lower thoracic spine (T10-11) (See particularly page 11, line 28-31). Etlinger et al. also teaches scoliosis may be caused by the neuromuscle weakness which is resulted from a spinal cord injury (See page 1, second paragraph).

The references do not expressly teach the dosage of clenbuterol as 0.5 to about 100  $\mu\text{g/kg}$  or about 40 $\mu\text{g/kg}$ .

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ 0.5 to about 100  $\mu\text{g/kg}$  or about 40 $\mu\text{g/kg}$  in the method of rehabilitation for spinal cord injury.

One of ordinary skill in the art would have motivated to employ 0.5 to about 100  $\mu\text{g/kg}$  or about 40 $\mu\text{g/kg}$  in the method of rehabilitation for spinal cord injury. The effect of clenbuterol in the instant method of treatment is known. As anyone of ordinary skill in the art will appreciate, preferred dosages are merely exemplary and serve as useful guideposts for the physician. There are, however, many reasons for varying dosages, including by orders of magnitude; for instance, an extremely heavy patient or one having an unusually severe infection would require a correspondingly higher dosage. Furthermore, it is routine during animal and clinical studies to dramatically vary dosage to obtain data on parameters such as toxicity and efficacy. Therefore, the optimization

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of result effect parameters (dosage range, dosing regimens) is obvious as being within the skill of the artisan, absent evidence to the contrary.

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, the experiment data of page 9-19 in the instant specification has been considered but are not found persuasive. The dosage of clenbuterol used in the experiment was 1.6mg/kg body wt/day, which is 1600µg/kg body wt. This dosage of clenbuterol was shown to be effective in treating spinal cord injury; however, it is outside the clenbuterol dosage range recited in the claims herein.

### ***Response to Arguments***

Applicant's arguments filed March 31, 2003 averring the dosage difference are considered moot in view of the new ground of rejection.

Applicant's arguments filed March 31, 2003 averring spinal cord contusion being different from scoliosis have been considered but are not found persuasive. Zeman et al. clearly teaches that clenbuterol is effective in treating spinal cord contusion injury.

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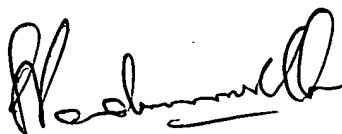
The declaration by Dr. Sansar C. Sharma filed March 31, 2003 have been considered but are not found persuasive to remove the outstanding rejections. The declaration merely points out what scoliosis is and its difference from spinal cord contusion injury. In view of the new ground of rejection, such remarks are considered moot.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui  
June 13, 2003

  
SREENI PADMANABHAN  
PRIMARY EXAMINER

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